



POLICY & PRACTICE

WANT MORE HEALTH REFORM NEWS?
SUBSCRIBE TO OUR PODCAST — SEARCH
'POLICY & PRACTICE' IN THE iTunes STORE

Society Backs Stem Cell Research

The Endocrine Society responded to a judge's temporary ban on federal funding for embryonic stem cell research by reiterating its call for more and broader funding for stem cell studies. Last month U.S. District Court Judge Royce Lamberth ruled that President Obama's 2009 expansion of federal funding violated a

1996 law making the destruction of human embryos illegal. Nevertheless, the Endocrine Society reissued its 2009 position statement backing increased National Institutes of Health funding for such research. The position paper also calls for more embryonic stem cell lines to be available for NIH-funded research and for funding of studies that use cells

Hypertriglyceridemia: Patients with fasting serum TG levels above 500 mg/dL were excluded from the diabetes clinical trials. In the phase 3 diabetes trials, 637 (63%) patients had baseline fasting serum TG levels less than 200 mg/dL, 261 (25%) had baseline fasting serum TG levels between 200 and 300 mg/dL, 111 (11%) had baseline fasting serum TG levels between 300 and 500 mg/dL, and 9 (1%) had fasting serum TG levels greater than or equal to 500 mg/dL. The median baseline fasting TG concentration for the study population was 172 mg/dL; the median post-treatment fasting TG was 195 mg/dL in the WELCHOL group and 177 mg/dL in the placebo group. WELCHOL therapy resulted in a median placebo-corrected increase in serum TG of 5% (p=0.22), 22% (p<0.001), and 18% (p<0.001) when added to metformin, insulin and sulfonylureas, respectively [See Warnings and Precautions (5.2) and Clinical Studies (14.2) in the full prescribing information]. In comparison, WELCHOL resulted in a median increase in serum TG of 5% compared to placebo (p=0.42) in a 24-week monotherapy lipid-lowering trial [See Clinical Studies (14.1) in the full prescribing information].

Treatment-emergent fasting TG concentrations ≥500 mg/dL occurred in 4.1% of WELCHOL-treated patients compared to 2.0% of placebo-treated patients. Among these patients, the TG concentrations with WELCHOL (median 604 mg/dL; interquartile range 538-712 mg/dL) were similar to that observed with placebo (median 644 mg/dL; interquartile range 574-724 mg/dL). Two (0.4%) patients on WELCHOL and 2 (0.4%) patients on placebo developed TG elevations ≥1000 mg/dL. In all WELCHOL clinical trials, including studies in patients with type 2 diabetes and patients with primary hyperlipidemia, there were no reported cases of acute pancreatitis associated with hypertriglyceridemia. It is unknown whether patients with more uncontrolled, baseline hypertriglyceridemia would have greater increases in serum TG levels with WELCHOL [See Contraindications (4) and Warnings and Precautions (5.2)].

Cardiovascular adverse events: During the diabetes clinical trials, the incidence of patients with treatment-emergent serious adverse events involving the cardiovascular system was 3% (17/566) in the WELCHOL group and 2% (10/562) in the placebo group. These overall rates included disparate events (e.g., myocardial infarction, aortic stenosis, and bradycardia); therefore, the significance of this imbalance is unknown.

Hypoglycemia: Adverse events of hypoglycemia were reported based on the clinical judgment of the blinded investigators and did not require confirmation with fingerstick glucose testing. The overall reported incidence of hypoglycemia was 3.0% in patients treated with WELCHOL and 2.3% in patients treated with placebo. No WELCHOL treated patients developed severe hypoglycemia.

6.2 Post-marketing Experience

The following additional adverse reactions have been identified during post-approval use of WELCHOL. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Drug Interactions with concomitant WELCHOL administration include:

- Increased seizure activity or decreased phenytoin levels in patients receiving phenytoin. Phenytoin should be administered 4 hours prior to WELCHOL.
- Reduced International Normalized Ratio (INR) in patients receiving warfarin therapy. In warfarin-treated patients, INR should be monitored frequently during WELCHOL initiation then periodically thereafter.
- Elevated thyroid-stimulating hormone (TSH) in patients receiving thyroid hormone replacement therapy. Thyroid hormone replacement should be administered 4 hours prior to WELCHOL [See Drug Interactions (7)].

Gastrointestinal Adverse Reactions

Bowel obstruction (in patients with a history of bowel obstruction or resection), dysphagia or esophageal obstruction (occasionally requiring medical intervention), fecal impaction, pancreatitis, abdominal distension, exacerbation of hemorrhoids, and increased transaminases.

Laboratory Abnormalities

Hypertriglyceridemia

7 DRUG INTERACTIONS

Table 4 lists the drugs that have been tested in *in vitro* binding or *in vivo* drug interaction studies with colesesevelam and/or drugs with postmarketing reports consistent with potential drug-drug interactions. Orally administered drugs that have not been tested for interaction with colesesevelam, especially those with a narrow therapeutic index, should also be administered at least 4 hours prior to WELCHOL. Alternatively, the physician should monitor drug levels of the co-administered drug.

Table 4
Drugs Tested in *In Vitro* Binding or *In Vivo* Drug Interaction Testing or With Post-Marketing Reports

Drugs with a known interaction with colesesevelam ^a	cyclosporine ^c , glyburide ^a , levothyroxine ^a , and oral contraceptives containing ethinyl estradiol and norethindrone
Drugs with postmarketing reports consistent with potential drug-drug interactions when coadministered with WELCHOL	phenytoin ^a , warfarin ^b
Drugs that do not interact with colesesevelam based on <i>in vitro</i> or <i>in vivo</i> testing	cephalexin, ciprofloxacin, digoxin, warfarin ^b , fenofibrate, lovastatin, metformin, metoprolol, pioglitazone, quinidine, repaglinide, valproic acid, verapamil

^a Should be administered at least 4 hours prior to WELCHOL

^b No significant alteration of warfarin drug levels with warfarin and WELCHOL coadministration in an *in vivo* study which did not evaluate warfarin pharmacodynamics (INR). [See Post-marketing Experience (6.2)]

^c Cyclosporine levels should be monitored and, based on theoretical grounds, cyclosporine should be administered at least 4 hours prior to WELCHOL.

In an *in vivo* drug interaction study, WELCHOL and warfarin coadministration had no effect on warfarin drug levels. This study did not assess the effect of WELCHOL and warfarin coadministration on INR. In postmarketing reports, concomitant use of WELCHOL and warfarin has been associated with reduced INR. Therefore, in patients on warfarin therapy, the INR should be monitored before initiating WELCHOL and frequently enough during early WELCHOL therapy to ensure that no significant alteration in INR occurs. Once the INR is stable, continue to monitor the INR at intervals usually recommended for patients on warfarin. [See Post-marketing Experience (6.2)]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B. There are no adequate and well-controlled studies of colesesevelam use in pregnant women. Animal reproduction studies in rats and rabbits revealed no evidence of fetal harm. Requirements for vitamins and other nutrients are increased in pregnancy. However, the effect of colesesevelam on the absorption of fat-soluble vitamins has not been studied in pregnant women. This drug should be used during pregnancy only if clearly needed.

In animal reproduction studies, colesesevelam revealed no evidence of fetal harm when administered to rats and rabbits at doses 50 and 17 times the maximum human dose, respectively. Because animal reproduction studies are not always predictive of human response, this drug should be used in pregnancy only if clearly needed.

8.3 Nursing Mothers

Colesesevelam hydrochloride is not expected to be excreted in human milk because colesesevelam hydrochloride is not absorbed systemically from the gastrointestinal tract.

8.4 Pediatric Use

The safety and effectiveness of WELCHOL as monotherapy or in combination with a statin were evaluated in children, 10 to 17 years of age with heFH [See Clinical Studies (14.1) in the full prescribing information]. The adverse reaction profile was similar to that of patients treated with placebo. In this limited controlled study, there were no significant effects on growth, sexual maturation, fat-soluble vitamin levels or clotting factors in the adolescent boys or girls relative to placebo [See Adverse Reactions (6.1)].

Due to tablet size, WELCHOL for Oral Suspension is recommended for use in the pediatric population. Dose adjustments are not required when WELCHOL is administered to children 10 to 17 years of age. WELCHOL has not been studied in children younger than 10 years of age or in pre-menarchal girls.

8.5 Geriatric Use

Primary Hyperlipidemia: Of the 1350 patients enrolled in the hyperlipidemia clinical studies, 349 (26%) were ≥65 years old, and 58 (4%) were ≥75 years old. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

generated by somatic cell nuclear transfer and those harvested from embryos discarded after *in vitro* fertilization procedures.

Diabetes Hospitalization Costs High

U.S. hospitals spent \$83 billion caring for people with diabetes in 2008, about 23% of the total for all conditions, according to the Agency for Healthcare Research and Quality. Nearly one in every five hospitalizations that year involved a patient with diabetes, the AHRQ said. The expenses included costs associated with more than 540,000 hospital stays specif-

ically for diabetes and roughly 7.2 million stays for diabetic patients being treated for other conditions such as heart disease, kidney damage, infection, and foot or leg amputation. On average, the AHRQ found, hospital stays for people with diabetes cost 25% more than did stays for people without the disease. Medicare paid 60% of the total bill for patients with diabetes, while private insurance paid 23% and Medicaid picked up 10% of the tab.

Diabetes, Environment Linked

Clean home environments and maternal obesity may be conducive to type 1 diabetes, researchers reported in the Archives of Pediatrics and Adolescent Medicine. Scientists based in Washington State and Israel compared nearly 1,900 children hospitalized with type 1 diabetes with more than 7,400 matched controls for factors involving maternal and child weights, family size, socioeconomic status, and prenatal care. They found that type 1 diabetes was less likely in children with older siblings and those with indicators of lower socioeconomic status. The researchers said that both associations lend credence to the hygiene hypothesis, which suggests that a cleaner living environment affects the developing immune system and causes increased susceptibility to autoimmune diseases.

Diabetes Education Helps

A study using data from private insurance and Medicare claims shows that people who receive diabetes education lasting more than a year have fewer inpatient hospital admissions and show higher compliance with medication regimens than do patients receiving less information about their disease. Commissioned by the American Association of Diabetes Educators and conducted by a consulting company, the study looked at 3 years of claims data. "Drug costs are higher and hospital admission costs are lower" for patients who receive the extended diabetes education, Karen Fitzner, Ph.D., chief science and practice officer for the association, said in an interview. Dr. Fitzner said that patients who have had more than a year of such training adhere to their treatment plans 2%-8% better than do those who haven't had any education.

Endocrinologist Satisfaction High

Endocrinologists remain highly satisfied with their career choice, with 76% saying they would choose the same career again and 73% saying they would recommend the field to a medical student, according to a survey by Epocrates, maker of mobile and Web-based information products. In the survey of 166 endocrinologists, nearly 70% said they spend more than 15 minutes with each patient. Responding to questions on a range of topics, they expressed some dislike for the new health care reform legislation, with 62% giving it a C or D and 20% giving it a failing grade. Almost 20% of the doctors said the new law would cause them to retire later, while 15% said it would result in their retiring earlier.

—Jane Anderson



Marketed by: Daiichi Sankyo, Inc. Parsippany, New Jersey 07054

P1801115